INTRODUCTION.

Proteolytic enzymes and their inhibitors have been studied for decades. The enzymes were among the first to be highly purified, crystallized and to have their structures determined by x-ray crystallography. Many of our modern concepts of enzyme specificity and enzyme mechanism have emergen from the study of proteolytic enzymes.

More recently we have entered another era in the investigation of proteolytic enzymes. It is now clear that proteolytic enzymes are involved in many important physiological processes such as blood coagulation, complement activation, fibrinolysis, kinin generation, fertilization, and hormone biosynthesis. Major breakthroughs are occurring constantly such as indica by recent research activity in the area of membrane proteolytic enzymes and their role in protein processing. Proteolysis now appears to be a major mechanism of biological control and has a significant role in morphogenesis and metamorphosis.

The study of natural inhibitors of proteolytic enzymes have led to a better understandi of several disease states. A correlation between emphysema and genetic difficiency of the plasma proteolytic enzyme inhibitor α_1-protease inhibitor (α_1-antitrypsin) led to investigation of proteolytic enzymes controlled by α_1-PI. It is now believed that the enzyme elastas from leukocytes causes the tissue destruction observed in emphysema. In addition evidence i now accumulating that cigarrette smoke is capable of oxidatively inactiviting α_1-PI with uncontrolled proteolysis of lung tissue by elastase then occurring. The metallo proteolytic enzyme collagenase probably plays a similar role in arthritis. This enzyme is also secreted by invasive tumors and is responsible for the destruction of connective tissue in the vicini of the tumor. Proteolysis is involved in chemical carcinogenesis, viral maturation, gonnoro and meningitis (the organisms secrete a proteolytic enzyme to cleave antibodies), bacterial infections (Pseudomonas aeruginosa strains with elastase are more virulent and cause lung hemorrages and corneal destruction), cystic fibrosis (a defect in the plasma proteolytic enzyme inhibitor α_2-macroglobulin has been speculated to be involved) and muscular distrophy

Synthetic and natural inhibitors are being developed to treat many of the above disease Bovine pancreatic trypsin inhibitor is currently on the market for the treatment of shock ar pancreatitis. An inhibitor of the angiotension converting enzyme is about to be marketed as a treatment for hypertension. In animals, elastase inhibitors are effective at controlling emphysema. A number of other protease inhibitors are being tested in animals for the treatment of a variety of diseases which include coagulation disorders, tumors and inflammation.

Gordon Conference. Two major meetings on "Proteases and Biological Control" (cold Spring Harbor, 1974) and "Protease Inhibitors" (Bayer Symposium, 1973) have covered the field or major aspects of the subject. Meetings on very specialized subjects ("The Physiological Inhibitors of Blood Coagulation and Fibrinolysis", 1978; "Neutral Proteases o Human Polymorphonuclear Leukocytes," 1977) occur quite frequently. Although the field of proteolytic enzymes and their inhibitors has generated considerable interest, no recent meetings that have been held have stimulated much interest, but there has never been any continuity.

The new Gordon Conference on "Proteolytic Enzymes and their Inhibitors" is being organi by Dr. James Travis (University of Georgia), Dr. Morris Zimmerman (Merck) and myself to pro vide a forum for discussion of recent advances in the field and to stimulate new research. We would hope that this Gordon Conference becomes established as a continuing forum for discussion in this rapidly developing field of research. A regular conference at two year intervals can easily be justified by the level of research in this field. The attached letters from scientists in a number of diverse research fields portray some of the enthusia that this proposed Gordon Conference has received.

Scientists working in the area of proteolytic enzymes and their inhibitors represent a number of diverse desciplines from organic chemistry to immunology. They are more likely t attend specialized meetings and never interact with each other. This Gordon Conference offers an opportunity for individulas with diverse backgrounds to get together and discuss subject of common interest. Discussions between scientists representing many disciplines a

of the general subject area. The meetings that have been held

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bound to stimulate future research in this area.

The major source of participants would be chemists and biochemists from academic institutions, government research laboratories such as NIH and industry (primarily pharmaceutical). The majority of the participants would have a basic science orientation, although a significant number would be clinically based.

Program and Speakers. The program for this new Gordon Conference is still in the planning stage since it was approved by the trustees of the Gordon Research Converences in early October 1979. The cochairman of the first conference will be Dr. James Powers (Georgia Institute of Technology) and Dr. James Travis (University of Georgia). In order to prepare a final program, we plan to solicite suggestions from the following scientists: Dr. Hans Neurath and Dr. Earl Davie (Dept. of Biochemistry, University of Washington), Dr. Morris Zimmerman (Merck Institute, New Jersey), Dr. Aaron Janoff (Dept. of Pathology, State University of N.Y. Stonybrook) and Dr. Michael Laskowski, Jr. (Dept. of Biochemistry, Purdue University). Attached is a tentative program and list of speakers. At present we have not had an opportunity to solicite suggestions from the above scientists and none of the speakers on following list have been contacted.

Budget

Airtravel for Speakers (Current Rates) (6141 International, 6298 Domestic)	$12,439
15% Expected Airfare Increase in Next 9 months	1,866
Conference fees for Speakers (includes Room & Board) - 35 x $200.	7,000
Bus (Boston to Conference and Return) 35 x $20.	700
	$22,005

Source of The Funds

Gordon Conference Special Fund	$ 5,500
Proposal Submited to NIH	5,000
Proposal Submitted to NSF	5,000
Proposal Submitted to Council for Tobacco Research	2,500
To be borne by Speakers	4,005
	$22,005

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Proteolytic Enzymes and Their Inhibitors
Proposed Program (Oct. 1979)

Session 1 - Structure and Function of Proteolytic Enzymes
Discussion Leader - Dr. Hans Neurath

	Subject Area	Travel (Est.)
Dr. Hans Neurath Biochem., Univ. of Wash. Seattle, WA	Proteolytic Enzymes Overview & Zymogen Activation	536
Dr. Bert Vallee Harvard Med. School Boston, Mass.	Metalloproteases	0
Dr. Theo Hoffman Biochem., Univ. Toronto Toronto, Canada	Acid Proteases	146
Dr. Michael James Biochem., Univ. of Alberta Alberta, Canda	X-ray Crystallographic Studies of bacterial Science Proteases	349

Session 2 - Structure and Function of Protease Inhibitors
Discussion Leader - Dr. Michael Laskowski, Jr.

Dr. Michael Laskowski, Jr. Dept. of Biochem., Purdue Univ. W. Lafayette, Indiana	Natural Protease Inhibitors	248
Dr. James Travis Biocher., Univ. of GA.	Plasma Protease Inhibitors	275
Dr. James C. Powers Chem., GA Tech. Atlanta, GA	Synthetic Substrates and Inhibitors of Enzymes	252
Dr. Peter Harpel Cornell Medical Center New York City	α_2-Macroglobulin	110
Dr. T. Ikenaka Osaka, Japan	α_1-Protease Inhibitor (α_1-antitrypsin)	1492

Session 3 - Coagulation and Fibrinolysis
Discussion Leader - Dr. Earl Davie

Dr. Earl Davie Dept. of Biochem., U. of Wash. Seattle, WA	Coagulation Serine proteases	536

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Dr. Elliott Shaw Biology, Brookhaven Nat. Lab. Upton, W.Y.	synthetic inhibitors of Trypsin-like enzymes	110
Dr. Robert Rosenberg Sidney Farber Cancer Center NYC	Antithrombin III	110
Lawrence Kress Roswell Park Memorial Inst.	Snake Verom proteases	152
D. Collen Univ. of Leuven Belgium.	Plasmin Inhibitor	945

Session 4 - Complement and Kinin Systems
Discussion Leader - Dr. Hans Fritz

Dr. Tony Hugli Res. Inst. of Scripps Clinic LaJolla, CA	Complement Proteases	552
Dr. David Bing Center for Blood Res. Boston, Mass.	Complement Proteases	0
Dr. Tadashi Inagani Biochem., Vanderbilt Nashville, Tenn.	Renin	252
Dr. John Pisano NIH Washington, DC		146
Dr. David W. Cushman Squibb New Jersey	Angiotension Converting Enzyme and Inhibitors	110
Dr. Art Patchett Merck Rahway, NJ	Angiotension Converting Enzyme and Inhibitors	110

Session 5 - Fertilization, Differentiation, Development, Viral Assembly
Discussion Leader - Dr. Kenneth Walsh

Dr. Kenneth Walsh Biochem., Univ. Wash. Seattle, Wash.	Sea Urchin Fertilization	536
Dr. Hans Fritz Munich Germany	Fertilization	800
Dr. Bruce Korant Central Research, DuPont Wilmington, Del.	Viral Proteases and Processing	114

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Dr. Kenneth Polakoski Wash. Univ. Sch. of Medicine St. Louis, MO	Acrosomal Proteases and Inhibitors	270

Session 6 - Protein Processing and Limited Proteolysis
Discussion Leader - Dr. Morris Zimmerman

Dr. Morris Zimmerman Merck Rahway, NJ	Membran Proteolytic Enzymes	110
Dr. Kenneth Walsh Dept. of Biochem., U. of Wash. Seattle, WA	Signal Peptidase	536
Dr. Gunter Blobel Rockefeller Univ. NYC	Signal Peptidase	110

Session 7 - Cellular Protein Turnover in the Normal and Diseased State
Discussion Leader - Dr. Alan J. Barrett

Dr. Alan J. Barrett Strangways Res. Lab. Cambridge, England	Proteases and Tissue Distruction	710
Dr. Hal Segal State Univ. of N.Y. Buffalo, N.Y.	Protein Turnover	152
Dr. T. Murachi Dept. of Clincial Sci., Kyoto Univ. Kyoto, Japan	Tissue Proteases	1492
Dr. C. B. Laurell Malmo Gen. Hospital Dept. of Clinical Chem., Maimo, Swedon	Plasma Protease Inhibitors in The Disease State	702

Session 8 - Poster Session
All participants of the Conference will be invited to present posters on their recent work.

Session 9 - Cellular Protein Turnover in the Normal and Diseased State
Discussion Leader - Dr. Aaron Janoff

Dr. Aaron Janoff Pathology, SUNY StoneyBrook, NY	Proteases and Emphysema	110
Dr. Ron Crystal NIHLBI Betheseda, Maryland	Proteases and Inhibitors in Lung Diseases	146

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Dr. Dan Rifkin Rockefeller University N.Y.C.	Proteases and Tumor Growth	110
Dr. Walter Troll Dept. Enviromental Medicine, NYU N.Y.C.	Proteases and Chemical Carcinogenesis	110

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